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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,606	11/10/2003	Lisa Benincosa	P32185C1	4699

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EXAMINER	
WILLIAMS, LEONARD M	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 06/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/705,606	BENINCOSA ET AL.	
	Examiner	Art Unit	
	Leonard M. Williams	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-14 and 16-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-14 and 16-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The examiner notes the preliminary amendment canceling claims 7 and 15 and amending claims 1, 3, 4, 5, 6, 8, 9, 10, 11, 12, 13, 14, 16, 17, 18, 19, and 20. Claim 21 is as originally presented.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 8-14 and 16-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Pool et al. (US Patent No. 5741803). as evidenced by Physician's Desk Reference (ed. 51, 1997, pages 1241-1244).

The examiner wishes to point out that the current specification discloses, on page 3, that compound (I)-the presently claimed compound-has a unit dose suitably comprising 2-12mg or preferably 4-8mg in a pharmaceutically acceptable form. The current specification discloses, on page 8, that the medicaments may be administered from 1-6 times a day, suitably 1 or 2 times a day, and preferably once a day.

Pool et al. teach, in col. 1 lines 10-25, compounds of formula (I) useful in the treatment and/or prophylaxis of Type II diabetes and related conditions including hyperlipidemia, hypertension and cardiovascular disease. Pool et al. teach, in col. 2 lines 40-45, a preferred compound of formula (I) is 5-[4-[2-(N-methyl-N-92-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione maleic acid (the maleic acid salt of the currently claimed compound). Pool et al. teach, in col. 5 lines 1-17, that the composition of formula (I) can be formulated for oral administration and can be delivered as unit dosages wherein the unit dose will normally contain an amount of the active ingredient in the range from 0.1-1000mg, and can be administered from 1-6 times a day anticipating the "...method for the treatment of Type 2 diabetes mellitus...method comprises the administration...of an effective non-toxic amount of an insulin sensitizer..." of claim1, the "...method...wherein the Threshold Plasma Concentration is within the range of from about 40 to about 200ng/nl" of claim 2, the "...method...wherein the Threshold Plasma Concentration is..." of claim 3, the "...method...wherein a minimum value of the Threshold Plasma Concentration...is its SC50 concentration" of claim 4, the "...method...wherein the preferred Threshold Plasma Concentration...is twice the SC50 concentration" of claim 5, the "...method...wherein the plasma concentration...remains...within the range of Minimum Threshold Plasma Concentration to a level at or above the Preferred Threshold Plasma Concentration" of claim 6, The "...method...wherein the SC50...is within the range of 40 to 65 ng/ml" of claim 8, the "...method...wherein the SC50 is 51.4ng/ml" of claim 9, the "...method...wherein the preferred threshold plasma concentration is in the range of about 80 to about 130 ng/ml

or about 82.2 to about 123.4 ng/ml" of claim 10, the "..method...wherein the preferred threshold plasma concentration is 100 ng/ml or 102.8 ng/ml" of claim 11, the "...method...wherein the plasma concentration...remains substantially within the range..." of claim 12, the "...method...wherein the plasma concentration...remains substantially at or above its preferred threshold plasma concentration" of claim 13, the "...method...wherein the plasma concentration of the insulin sensitizer remains at or above 100ng/ml..." of claim 14, the "...pharmaceutical composition comprising an insulin sensitizer...and a pharmaceutically acceptable carrier..." of claim 16, the "...pharmaceutical composition...wherein the composition is adapted to provide a plasma concentration of the insulin sensitizer..." of claim 17, the "...modified release pharmaceutical composition..." of claims 18 and 19, and the "...composition...adapted to provide a method of treatment..." of claim 20.

Claim 21 is rejected as being anticipated by Pool et al. as evidenced by the Physicians desk reference. Pool et al is as set forth above. Pool does not teach explicitly the method by which the threshold plasma concentration for a given antidiabetic compound can be determined as set forth in current claim 21. The PDR teaches on page 1242 the pharmacodynamics, and pharmacokinetics of an antidiabetic drug called glimepiride. Glimepiride is shown to have a glucose-lowering effect wherein the time to reach maximum effect via oral dosages was about 2-3 hrs. Blood glucose and HbA1c were found to respond in a dose-dependant manner over a range of 1 to 4 mg/day. The table at the bottom of page 1242 shows the pharacokinetic parameters of glimepiride from a single-dose, cross over, dose-proportionality study in normal subjects

and in patients with NIDDM. It clearly indicates that glimepiride did not accumulate in the serum. The testing performed for glimepiride is indicative of studies required by the FDA for the pharmacokinetics of any drug. Thus the determination of threshold plasma concentration for any given drug is routinely done and is required to be done as part of the drug development process.

The examiner respectfully points out the following: "Products of identical chemical composition can not have mutually exclusive properties. "A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over pool et al. as applied to claims 1-6, 8-14 and 16-20 above, and further in view of The Physicians Desk Reference (1997, 51 ed., pages 1241-1244).

Pool et al. is as set forth above.

Pool does not teach explicitly the method by which the threshold plasma concentration for a given antidiabetic compound can be determined as set forth in current claim 21. The PDR teaches on page 1242 the pharmacodynamics, and pharmacokinetics of an antidiabetic drug called glimepiride. Glimepiride is shown to have a glucose-lowering effect wherein the time to reach maximum effect via oral dosages was about 2-3 hrs. Blood glucose and HbA1c were found to respond in a dose-dependant manner over a range of 1 to 4 mg/day. The table at the bottom of page 1242 shows the pharmacokinetic parameters of glimepiride from a single-dose, cross over, dose-proportionality study in normal subjects and in patients with NIDDM. It clearly indicates that glimepiride did not accumulate in the serum. The testing performed for glimepiride is indicative of studies required by the FDA for the pharmacokinetics of any drug. Thus the determination of threshold plasma concentration for any given drug is routinely done and is required to be done as part of the drug development process. One would be motivated to determine the threshold plasma concentration, by any acceptable means, in order to comply with the federal guidelines as detailed in the PDR above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LMW

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER